Prevalence of pulmonary tuberculosis in western China in 2010–11: a population-based, cross-sectional survey

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Summary

Background Progress in tuberculosis control in China has been the slowest in western areas, which have the highest prevalence. We assessed the prevalence of pulmonary tuberculosis in the Xinjiang province, China, 10 years after introduction of a control programme based on directly observed treatment, short course.

Methods In this population-based, cross-sectional survey, we used a multistage stratified random cluster sample design to estimate the prevalence of smear-positive and bacteriologically confirmed (either smear positive or culture positive, or both) pulmonary tuberculosis among adults (aged ≥15 years) in Xinjiang who had been resident in their household for the last 6 months. The screening strategy and diagnosis followed WHO guidelines. We estimated prevalence by combining inverse probability weighting and multiple imputation of missing data. We compared our prevalence survey estimates with the ones from the 2010 China national pulmonary tuberculosis survey and the ones from a provincial pulmonary survey done in Xinjiang in 2000. The new smear-positive pulmonary tuberculosis notification rate in 2011 in Xinjiang was obtained to allow the calculation of patient diagnosis rate (PDR).

Findings Between Sept 1, 2010, and July 31, 2011, 31 081 individuals were eligible, of whom 29 835 (96·0%) participated in the survey. We identified 50 (0·2%) smear-positive and 101 (0·3%) bacteriologically confirmed pulmonary tuberculosis cases. The weighted prevalence of smear-positive pulmonary tuberculosis was 170 (95% CI 103–233) per 100 000 people and of bacteriologically confirmed pulmonary tuberculosis was 430 (249–611) per 100 000 people. Compared with 2000 Xinjiang survey estimates, the prevalence of smear-positive pulmonary tuberculosis has decreased by 26·4% (from 231 [95% CI 148–314] per 100 000 people), whereas the prevalence of bacteriologically confirmed pulmonary tuberculosis has increased by 17·8% (from 365 [237–493] per 100 000 people). In each age group and sex, the pulmonary tuberculosis prevalence was higher in the 2010–11 Xinjiang survey than in the 2010 national survey. The PDR in 2011 was 0·34 (95% CI 0·25–0·44).

Interpretation Despite progress in other parts of China, the prevalence of pulmonary tuberculosis in Xinjiang remains high. The very low PDR suggests poor access to diagnosis and care. Further studies are needed to understand the barriers to diagnosis and care of this population, and efforts are urgently needed to enhance tuberculosis screening in this area.

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See Comment page e434

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Introduction

Tuberculosis remains a major global health problem, responsible for ill health among millions of people each year, particularly in low-income and middle-income countries. Of the estimated 9·6 million people who developed tuberculosis globally in 2014, India accounted for 23% and China accounted for 10%.[1] During the past two decades, China has implemented a large-scale tuberculosis control programme to address its growing tuberculosis problem. This programme is based on directly observed treatment, short course (DOTS), and was implemented in 13 provinces of China in the 1990s and expanded nationwide after 2000.[2] Analysis of the 2010 national pulmonary tuberculosis prevalence survey in China indicated that scale-up of the DOTS strategy in China led to a decline in the prevalence of smear-positive pulmonary tuberculosis by 48% and bacteriologically confirmed pulmonary tuberculosis by 65% between 1990 and 2010.[3] However, the smallest declines occurred in western provinces (Chongqing, Gansu, Guangxi, Guizhou, Neimeng, Ningxia, Qinghai, Shanxi, Sichuan, Tibet, Xinjiang, and Yunnan), where the pulmonary tuberculosis prevalence was the greatest.[4]

The Xinjiang Uyghur Autonomous Region (Xinjiang) is located in northwestern China, with international borders with Russia, Mongolia, Kazakhstan, Kyrgyzstan, Tajikistan, Afghanistan, Pakistan, and India, with a population of 20 million people and 13 ethnic minorities. It is one of the provinces known to have a high burden of tuberculosis. A pulmonary tuberculosis survey done in Xinjiang in 2000 showed that the prevalence of smear-positive pulmonary tuberculosis among adults (aged ≥15 years) was 231 per 100 000 people and of bacteriologically confirmed tuberculosis was 365 per 100 000 people.[5,6] The DOTS strategy was introduced in some counties in Xinjiang in the 1990s and expanded to the whole region after 2000.

The effect that DOTS has had on the burden of pulmonary tuberculosis in Xinjiang was not clear from

Research in context

Evidence before this study

We searched MEDLINE, Embase, Google Scholar, and some key Chinese databases WanFang and ZhiWang for studies published from Jan 1, 1945, to Oct 20, 2015, with the search terms "tuberculosis", "pulmonary tuberculosis", "infectious disease", "survey", "provincial survey", "prevalence", "China", and "Asia". We searched for studies published in Chinese in the Chinese databases and those published in English in the other databases. To maintain relevance to current efforts in tuberculosis care and control and given that 1990 is the baseline year for 2015 global tuberculosis targets, we focused on national surveys done between 1990 and 2012 in Asia and provincial surveys done in China. Globally, 21 surveys were done in 12 countries, and published results were available for 18. Four countries (China, Cambodia, South Korea, and the Philippines) have repeated national surveys since 1990 and have shown declines in the prevalence of smear-positive and bacteriologically confirmed pulmonary tuberculosis by 50% over 10 years. In China, the Ningxia, Gansu, Guangdong, Henan, Jiangsu, and Shandong provinces did separate provincial surveys after the fifth China national pulmonary tuberculosis survey in 2010. The prevalence of bacteriologically confirmed pulmonary tuberculosis among adults aged 15 years or older was similar in Ningxia, Gansu, Guangdong, Henan, and Jiangsu (range 63 per 100 000 people to 79 per 100 000 people) and lowest in Shandong (30 per 100 000 people). These provinces have also done repeated provincial surveys since the 1990s, and all reported that the prevalence of both smear-positive and bacteriologically confirmed pulmonary tuberculosis has declined by more than 50% since the 1990s.

Added value of this study

This study provides new data on the burden of pulmonary tuberculosis in the Xinjiang province of western China. The results show that the prevalence of pulmonary tuberculosis is quite high in Xinjiang compared with other parts of China. Ethnic minorities, men, and those living in rural southern Xinjiang are at an increased risk. A small decline in smear-positive prevalence and a small increase in bacteriologically confirmed prevalence after implementation of DOTS-based tuberculosis control programmes for 10 years indicates that progress in tuberculosis control in western China has been small.

Implications of all the available evidence

Although China has achieved a 50% reduction in pulmonary tuberculosis prevalence nationally since the 1990s, regional disparities are large, and the burden of tuberculosis in western China remains high. Low case detection rates with DOTS indicate that a substantial number of tuberculosis cases in western China are still undetected, meaning that DOTS might not be effectively implemented in western China where people, health infrastructure, and human resources in tuberculosis care are poor.

the 2010 national survey as only three of the survey clusters (roughly 1500 participants per cluster) were from Xinjiang, a sample size too small to produce precise estimates. Therefore, a population-based pulmonary tuberculosis prevalence survey with more extensive sampling was done by the Xinjiang Uyghur Autonomous Region Health Bureau (or Health and Family Planning Commission of Xinjiang Uyghur Autonomous Region after 2015) and Xinjiang Center for Disease Control and Prevention (CDC) to measure more precisely the burden of pulmonary tuberculosis in Xinjiang than the 2010 survey. Preliminary findings were reported by Yang and colleagues.[6] In this report, we present a more detailed analysis than that of Yang and colleagues of the prevalence of smear-positive and bacteriologically confirmed pulmonary tuberculosis and the demographic determinants of bacteriologically confirmed pulmonary tuberculosis. We also report the patient diagnosis rate (PDR), an indicator of case detection performance of tuberculosis control programmes.[7,8]

Methods

Study design

In this population-based, cross-sectional survey, we estimated the prevalence of smear-positive and bacteriologically confirmed pulmonary tuberculosis in adults (aged ≥15 years) in Xinjiang using a multistage stratified random cluster sample design. To confirm local residency and to exclude the mobile population, we considered all adults who had been resident in their household for at least the last 6 months eligible for survey participation. We stratified the province into urban (cities), semi-urban (towns), and rural areas (townships). We allocated six clusters to urban areas, seven to semi-urban areas, and nine to rural areas, which was proportional to the population of each stratum.[9] We defined a cluster as a community (defined by postal code) in a city, town, or village in a township. Within each stratum, we first selected cities, towns, or townships with probability proportional to size. Within the selected cities or towns, we first selected streets with probability proportional to size and then communities within streets with simple random sampling done with Stata 13.0, assuming that communities within the same street have similar population sizes. Within the selected townships, we selected villages with simple random sampling with Stata 13.0 on the basis of the same assumption above. This method gave an approximately self-weighting design. In each community or village, we visited all households. If the population of eligible individuals in a cluster was fewer than 1500 people, then we added part of the next adjoining village or community to reach the target size. If the population of eligible individuals in a cluster was higher than the target size, then we included all those eligible. Participants were those who took part in at least one of the screening methods (symptom or radiograph screening). The Xinjiang Uyghur Autonomous Region Health Bureau and the Office of the Fifth Provincial Pulmonary Tuberculosis Survey gave ethical approval for this survey.

Procedures

We formed ten survey teams, each of which was responsible for investigating two to three survey clusters. Each survey team consisted of three fieldworkers, four physicians, two radiologists, three data managers, and two laboratory technicians. Before the survey, all survey team staff were trained in survey objectives, interview procedures, standard operation procedures for sputum collection and testing, and pulmonary tuberculosis diagnosis criteria. We obtained a list of all households from the local household registration office, and then we carried out a population census of the survey cluster by visiting each household. We invited eligible individuals identified during the census for pulmonary tuberculosis screening at the local clinics, which served as the central survey sites.

At the survey clinic, the aims of the survey and the procedures involved were explained and signed consent was sought. Those who consented were screened for pulmonary tuberculosis symptoms by a local medical officer using a short questionnaire and had a posteroanterior chest radiograph (unless they were pregnant or disabled). All chest radiographs were immediately read by a radiologist. We defined an abnormal chest radiograph as one showing any lung abnormality (ie, opacities, cavitations, fibrosis, pleural effusion, calcification, or any unexplained or suspicious shadow). We considered participants who reported cough or sputum production for at least the past 2 weeks (via the questionnaire), participants with haemoptysis (via the questionnaire), and participants who had an abnormal chest radiograph to have presumptive pulmonary tuberculosis. For quality assurance, all abnormal chest radiographs and a randomly selected 10% of chest radiographs reported as normal (random selection with Stata 13.0) were reread by a senior radiologist from Xinjiang Medical University First Affiliated Hospital (Ürümqi, Xinjiang, China) for a final decision.

All participants with presumptive pulmonary tuberculosis were requested to submit three sputum specimens (on the spot, the same evening, and early in the morning on the following day). Clear instructions on how to produce a good sputum specimen were given to all participants with presumptive pulmonary tuberculosis by survey technicians before specimen collection. If a specimen was not satisfactory for laboratory investigation, the participant was asked to produce a repeat (evening or morning) specimen. Eligible individuals who were unable to visit the survey clinic (those who were disabled or pregnant) were visited by survey team staff in their homes, where they were interviewed with questions about pulmonary tuberculosis symptoms and requested to submit three sputum specimens, irrespective of the presence of pulmonary tuberculosis symptoms.

Sputum specimens were transported to laboratories closest to investigation sites with use of cold-chain logistics, and all three sputum specimens from each participant with presumptive pulmonary tuberculosis were tested for acid-fast bacilli (AFB) with Ziehl-Neelsen smear microscopy. Two sputum specimens from each participant with presumptive pulmonary tuberculosis were selected on the basis of degree of smear positivity or sputum quality and cultured with Löwenstein-Jensen medium. Smear examination and culturing were done within 5 days of sputum collection. Local laboratory technicians were experienced and well trained before the survey, and all were required to follow the same standard operation procedures described in the survey protocol. Additionally, the provincial reference laboratory closely monitored the quality of sputum culture. Cultures with growing colonies were sent to the provincial reference laboratory for identification and drug susceptibility testing. Growth characteristics, morphological characteristics of the colony, and p-nitrobenzoic acid inhibition testing were used to differentiate a *Mycobacterium tuberculosis* complex from a non-tuberculosis mycobacterium. All AFB-positive and a randomly selected 10% of AFB-negative smears (random selection with Stata 13.0) were reread by the central review panel at the provincial reference laboratory.

We defined a participant with a smear-positive diagnosis as having at least two sputum smears positive for AFB (we defined AFB positive as at least one AFB in 100 fields), having one sputum smear positive for AFB and one sputum culture positive for *M tuberculosis* (defined as at least one colony of *M tuberculosis* complex isolated), or having one sputum smear positive for AFB and an abnormal chest radiograph. We defined a participant with a culture-positive diagnosis as having at least one sputum culture positive for *M tuberculosis*. A participant with a bacteriologically confirmed case had a smear-positive or culture-positive diagnosis, or both. We defined a participant with a new diagnosis as one who had never been treated for pulmonary tuberculosis or who had taken antituberculosis drugs for less than a month. We defined a participant with a previously treated diagnosis as one who had taken antituberculosis drugs for more than a month at some time in the past.

Statistical analysis

We calculated the sample size to give a relative precision of 30% for the estimated smear-positive pulmonary tuberculosis prevalence, assuming a design effect of 1·4 and that 90% of the eligible population would

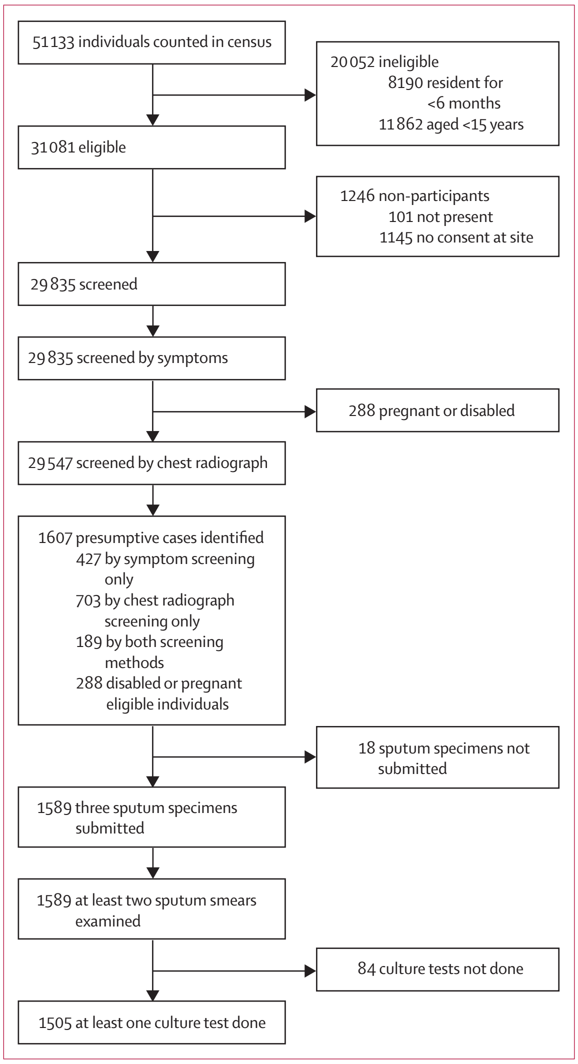

Figure 1: Flow chart of survey participants

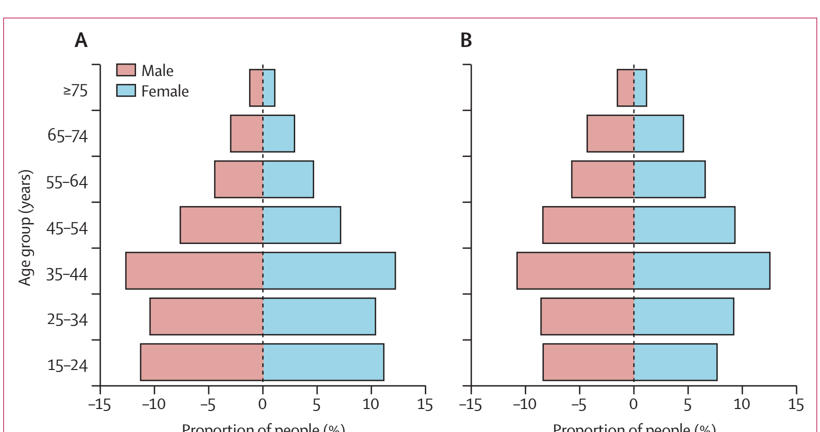

Figure 2: Age and sex distribution of (A) the general population of Xinjiang (2011 estimate) and (B) the participating population in our Xinjiang pulmonary tuberculosis prevalence survey in 2010–11

participate and that the anticipated prevalence would be equal to 85% of that estimated in the 2000 Xinjiang survey. On the basis of these assumptions, 22 clusters of 1500 individuals—a total of 33 000—were required.

We recorded data using software (China national tuberculosis survey data recording software) designed by China CDC for the China national pulmonary tuberculosis survey in 2010 and for use in subsequent provincial pulmonary tuberculosis surveys. We analysed data with Stata version 13.0. The analysis of survey results followed the guidelines recommended in the WHO tuberculosis prevalence survey handbook,[10] which provides methods to be used for self-weighting surveys with a constant sample size per cluster. We did complete case analysis (method one) and individual-level analysis combining inverse probability weighting with multiple imputation of missing data (method two) to estimate the prevalence of smear-positive and bacteriologically confirmed pulmonary tuberculosis with a logistic regression model. In method one, we estimated the crude prevalence of pulmonary tuberculosis, restricting analysis to survey participants with results and excluding those with presumptive pulmonary tuberculosis whose smear or culture results were missing. In method two, we estimated the weighted prevalence of pulmonary tuberculosis. We estimated 95% CIs with robust SEs for both methods. This analysis accounted for the cluster sample survey design and corrected for potential bias due to missing data. We did this correction using the svy, mim, and ice commands in Stata. Additionally, we estimated specific prevalence by survey strata, age group, sex, ethnic group, and geographical location using both methods. These two analysis methods are described elsewhere in detail.[11]

We did multiple imputation of missing smear and culture results using regression models with the imputation-by-chained-equations procedure, which makes the assumption that the data were missing at random.[12] We included age 15–24 years, 25–34 years, 35–44 years, 45–54 years, 55–64 years, and 65–74 years; female sex; Uyghur ethnicity; Han ethnicity; urban (yes or no); semi-urban (yes or no); chest radiograph abnormality (yes or no); and presence of cough for at least the past 2 weeks (yes or no) in the imputation models. We did multiple imputation of missing data only for participants with presumptive pulmonary tuberculosis. Participation varied by age, sex, and cluster in this survey, therefore unweighted analysis could be biased. We used inverse probability weighting to correct for differentials in participation by age, sex, and cluster. Additionally, we did multivariate logistic regression analysis to assess demographic determinants of bacteriologically confirmed pulmonary tuberculosis. We estimated crude and adjusted prevalence odds ratios with 95% CIs. As pulmonary tuberculosis prevalence is low, the prevalence odds ratio closely approximates the prevalence ratio. As a comparison, we estimated the adjusted prevalence ratios using generalised linear modelling and proportional hazards regression (appendix).[13]

We calculated the PDR as the number of newly reported cases (excluding treated patients) of smear-positive pulmonary tuberculosis per 100 000 people per year divided by the survey estimate of the prevalence of new cases of smear-positive pulmonary tuberculosis per 100 000 people.[7] We calculated a 95% CI for the PDR using an SE for the log PDR obtained by the δ method, giving confidence limits of the PDR calculated as PDR/EF to PDR × EF,

$$EF = exp \times (1 \cdot 96 \times \sqrt{\frac{1}{c} + \left(\frac{se_p}{p}\right)^2})$$

where c is the number of notified new smear-positive pulmonary tuberculosis cases, p is the survey estimate of the smear-positive pulmonary tuberculosis prevalence, and se_p is its SE. We compared the prevalence of smear-positive and bacteriologically confirmed pulmonary tuberculosis in each age group in this survey (age and sex standardised to the total population of China in 2010) with that estimated in the 2010 national survey. We also compare the prevalence of smear-positive and bacteriologically confirmed pulmonary tuberculosis in this survey with the ones from a provincial pulmonary survey done in Xinjiang in 2000.

See Online for appendix

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The Xinjiang CDC operates under the general guidance of the Xinjiang Uyghur Autonomous Region Health Bureau and was responsible for the survey design, field investigation, and data collection. LY, XF, and HU had full access to all the data in the study and had final responsibility for the decision to submit for publication.

	Crude*	Weighted†
Overall	168 (114–222)	170 (103–233)
Stratum		
Urban	36 (7–65)	35 (3–67)
Semi-urban	247 (175–318)	247 (170–324)
Rural	199 (129–268)	198 (115–281)
Sex		
Male	243 (170–315)	241 (163–319)
Female	97 (41–154)	98 (36–160)
Age group (years)		
15–24	124 (23–225)	121 (20–222)
25–34	223 (104–343)	225 (100–350)
35–44	85 (12–158)	85 (11–159)
45–54	168 (28–309)	170 (26–314)
55–64	242 (30–454)	245 (27–463)
65–74	224 (41–406)	225 (31–419)
≥75	246 (27–465)	258 (3–513)
Ethnic group		
Han	38 (5–71)	37 (3–71)
Uyghur	247 (188–307)	248 (185–311)
Other	217 (126–309)	216 (130–302)
Geographical location		
Eastern region	71 (13–129)	72 (11–133)
Northwestern region	129 (71–187)	128 (66–190)
Southern region	244 (172–316)	245 (170–320)

*Uses logistic regression with robust SEs, without missing value imputation or inverse probability weighting. †Uses logistic regression with robust SEs, combining missing value imputation and inverse probability weighting.

Table 1: **Prevalence of smear-positive pulmonary tuberculosis in Xinjiang per 100 000 people (95% CI)**

	Prevalence per 100 000 people (95% CI)		Crude POR (95% CI)	Adjusted POR (95% CI)	p value
	Crude*	Weighted†			
Overall	342 (206–477)	430 (249–611)	..	..	..
Stratum					
Urban	107 (44–170)	109 (38–180)	1	1	..
Semi-urban	413 (223–604)	613 (162–1065)	5·65 (1·93–16·55)	2·05 (0·98–4·32)	0·057
Rural	451 (206–695)	506 (253–759)	4·66 (1·92–11·30)	2·27 (1·01–5·12)	0·048
Sex					
Male	426 (298–554)	519 (327–712)	1	1	..
Female	262 (99–425)	341 (143–538)	0·66 (0·40–1·07)	0·69 (0·32–0·86)	0·036
Age group (years)					
15–24	187 (82–292)	244 (64–424)	1	1	..
25–34	319 (142–495)	386 (177–595)	1·59 (0·54–4·66)	1·71 (1·26–5·16)	0·031
35–44	100 (23–176)	119 (30–208)	0·49 (0·14–1·67)	0·72 (0·20–2·61)	0·579
45–54	226 (44–407)	277 (62–491)	1·14 (0·37–3·47)	1·65 (0·52–5·22)	0·361
55–64	626 (197–1055)	707 (190–1223)	2·91 (1·01–8·38)	4·13 (1·40–12·18)	0·016
65–74	992 (370–1615)	1295 (541–2050)	5·37 (2·07–13·98)	10·09 (3·79–26·87)	0·001
≥75	889 (35–1744)	1249 (130–2369)	5·18 (1·43–18·82)	9·70 (2·45–38·47)	0·004
Ethnic group					
Han	95 (42–148)	98 (42–155)	1	1	..
Uyghur	537 (328–745)	673 (354–993)	6·88 (3·10–15·30)	6·28 (3·20–12·36)	<0·0001
Other	331 (179–484)	444 (191–699)	4·54 (2·03–10·14)	4·34 (2·26–8·35)	<0·0001
Geographical location‡					
Eastern region	143 (49–236)	144 (50–237)	1	..	..
North-western region	162 (92–233)	189 (88–290)	1·31 (0·51–3·39)	..	..
Southern region	571 (363–779)	739 (417–1061)	5·17 (2·15–12·44)	..	..

POR=prevalence odds ratio. *Uses logistic regression with robust SEs, without missing value imputation or inverse probability weighting. †Uses logistic regression with robust SEs, combining missing value imputation and inverse probability weighting. ‡Geographical location is not included in the multivariate logistic regression model because of colinearity with ethnic group.

Table 2: **Prevalence of bacteriologically confirmed pulmonary tuberculosis in Xinjiang per 100 000 people**

Results

Between Sept 1, 2010, and July 31, 2011, 51 133 individuals were counted during the survey (figure 1). Of these, we considered 31 081 (60·8%) eligible for survey participation and invited them for pulmonary tuberculosis screening. Of these, 29 835 (96·0%) participated in at least one of the screening methods. Participants in this survey were slightly older than were the general population of Xinjiang (figure 2). Of them, 13 761 (46·1%) were Uyghur, 10 554 (35·4%) were Han, and 5520 (18·5%) were of other ethnicities, which is similar to the proportion of ethnic groups in the total population of Xinjiang.[9] 1246 (4·0%) eligible individuals did not participate in screening. Non-participation was slightly higher in men (636 [4·2%] of 15 074) than in women (610 [3·8%] of 16 007) and was the highest in those aged 75 years or older (64 [7·3%] of 876), followed by those aged 15–24 years (298 [5·8%] of 5145), and 25–34 years (254 [4·5%] of 5626). Non-participation was similar between Han (450 [4·1%] of 11 005)], Uyghur (557 [3·9%] of 14 318) and others (239 [4·2%] of 5758), and between urban (377 [4·3%] of 8782), semi-urban (366 [3·8%] of 9692), and rural areas (503 [4·0%] of 12 607).

Of the 1505 participants who had a sputum culture test done, *M tuberculosis* positivity was confirmed by at least one sputum culture for 1346 (89·4%), both cultures were contaminated for 145 (9·6%), and non-tuberculosis mycobacterium was confirmed by both culture results for 14 (0·9%; two [0·1%] smear positive and 12 [0·8%] smear negative). 1245 (78·4%) of the 1589 participants who had at least two sputum smears examined were smear negative and culture negative and 84 (5·3%) were smear negative and did not have culture testing done. The central review panel identified 101 (6·4%) bacteriologically confirmed cases of the 1589 participants who had at least two sputum smears examined. Of them, 50 (49·5%) were smear-positive cases and 94 (93·1%) were culture-positive cases. Of 50 smear-positive cases, 43 (86·0%) were culture positive and seven (14·0%) were culture negative. Of 94 culture-positive cases, 51 (54·3%) were smear negative.

Of 50 participants with smear-positive results, 28 (56·0%) reported cough or sputum production for at least the past 2 weeks or haemoptysis, and 47 (94·0%) had abnormal chest radiographs. Of 101 bacteriologically confirmed cases, 52 (51·5%) reported cough or sputum production for at least the past 2 weeks or haemoptysis and 90 (89·1%) had abnormal chest radiographs. Of 101 bacteriologically confirmed cases, 24 (23·8%) had been previously diagnosed and notified to the Chinese tuberculosis surveillance system before the survey. Among 24 participants with a previous diagnosis, 18 (75·0%) were being treated at the time of screening, four (16·7%) had a history of receiving incomplete treatment before the survey, and two (8·3%) were previously diagnosed but had never received treatment.

Estimates of the prevalence of smear-positive and bacteriologically confirmed pulmonary tuberculosis are shown in table 1 and table 2. The crude prevalence of smear-positive pulmonary tuberculosis was 168 (95% CI 114–222) per 100 000 people and of bacteriologically confirmed pulmonary tuberculosis was 342 (206–477) per 100 000 people. Geographically, the crude prevalence was highest in the southwestern prefectures of the province (figure 3). The weighted prevalence of smear-positive pulmonary tuberculosis was 170 (103–233) per 100 000 people and of bacteriologically confirmed tuberculosis was 430 (249–611) per 100 000 people (table 1, table 2). The design effect was 1·79 for smear-positive pulmonary tuberculosis and 3·50 for bacteriologically confirmed pulmonary tuberculosis. The coefficient of between-cluster variation (k) was 0·59 for smear-positive pulmonary tuberculosis and 0·65 for bacteriologically confirmed pulmonary tuberculosis.

The weighted prevalence of smear-positive and bacteriologically confirmed pulmonary tuberculosis was higher in young adults aged 25–34 years and in those aged older than 54 years (table 1, table 2). In each age group, the prevalence was higher in men than in women and was higher in this 2010–11 Xinjiang survey than in the 2010 national survey (figure 4, figure 5). Additionally, the weighted prevalence of bacteriologically confirmed pulmonary tuberculosis was substantially higher in semi-urban and rural areas, the Uyghur ethnic group, and the southern region (table 2).

The major characteristics and results of the 2000 Xinjiang survey and this 2010–11 survey are shown in table 3. Compared with the 2000 pulmonary tuberculosis survey in Xinjiang, the prevalence of smear-positive pulmonary tuberculosis in adults has declined

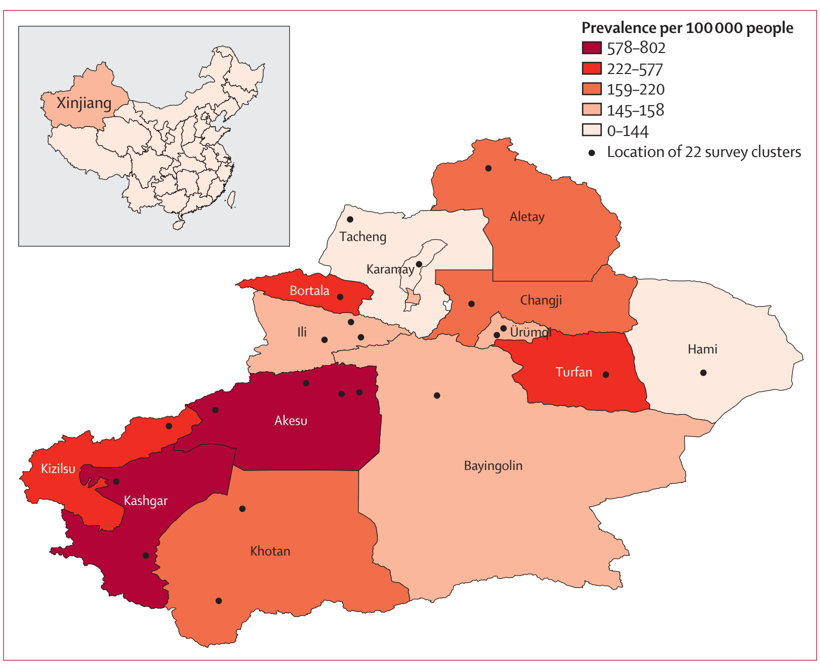

Figure 3: Crude prevalence of bacteriologically confirmed pulmonary tuberculosis in 14 prefectures of Xinjiang in 2010–11 by 26·4%, whereas the prevalence of bacteriologically confirmed pulmonary tuberculosis has increased by 17·8%. The overall PDR in 2011 was only slightly higher than that in 2000. The PDR in 2011 was substantially lower in men, young adults aged 25–34 years, and among the Uyghur ethnic group (table 4). It was also lower in semi-urban and rural areas than in urban areas and in the southern region than in other regions.

Discussion

Findings from this survey show that the prevalence of pulmonary tuberculosis in the Xinjiang province remained high even after DOTS-based tuberculosis control programmes had been in place for longer than 10 years. Although the prevalence of smear-positive pulmonary tuberculosis seems to have decreased in Xinjiang since the 2000 survey, the decrease is less than half of that observed in the same period nationally (26% *vs* 57%).[3] The increase in the prevalence of bacteriologically confirmed pulmonary tuberculosis could reflect a real increase, but could also be due to underestimation of the prevalence in the 2000 survey. In the 2000 survey, the criteria used for symptom screening were cough or sputum production for at least the past 3 weeks, and fluoroscopy was used for chest radiograph screening,[6,14] both of which are less sensitive for identification of presumptive pulmonary tuberculosis than are the methods used in this survey. Nonetheless, the results of our survey suggest that progress in tuberculosis control has been slow in western China and the burden of tuberculosis remains extremely high.

Despite the fact that prevalence has declined by more than half in the past two decades in China overall, regional disparities are large. Findings from the 2010 China national survey indicated that the prevalence of bacteriologically confirmed pulmonary tuberculosis among adults in the western region of China was 1·7 times higher than that in the central region and 3·2 times higher than that in the eastern region.[15] And within western China, the prevalence among adults in Xinjiang in 2010–11 from our survey was higher than the average prevalence in the western region estimated in the 2010 national survey. Furthermore, findings from our survey show a regional disparity in prevalence within the province. The prevalence of bacteriologically confirmed pulmonary tuberculosis was higher in the southern region of Xinjiang than in the northern and eastern regions and was higher in semi-urban and rural areas than in urban areas. These disparities reflect the levels of economic development. Regions with slow economic development tend to have few financial resources, few qualified health-care workers, and weak public health infrastructure, which are known to be associated with high tuberculosis burden.[16,17] Additionally, poverty, a well known risk factor for tuberculosis, is more widespread in the underdeveloped, western region of China and the southern region of Xinjiang than in other areas.[18] National tuberculosis control programmes should focus

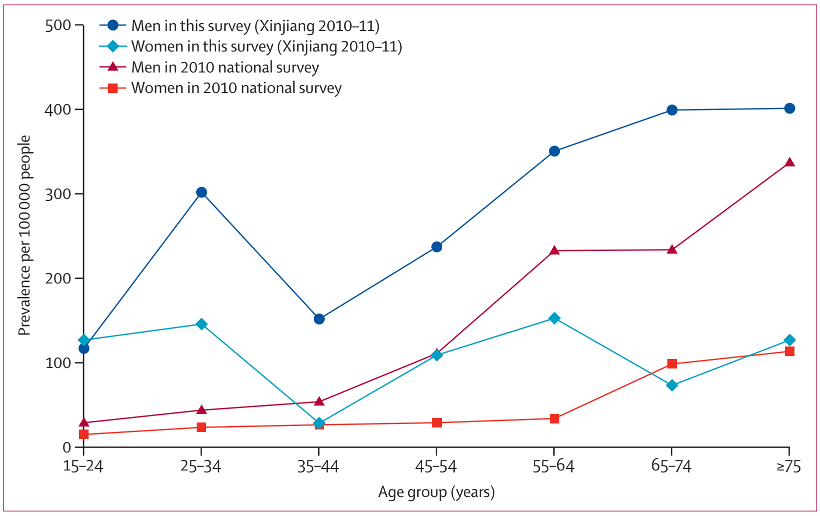

***Figure 4*: Age-specific prevalence of smear-positive pulmonary tuberculosis stratified by sex in our Xinjiang survey and the 2010 national survey**
Prevalence in this survey age and sex standardised to the population of China in 2010.

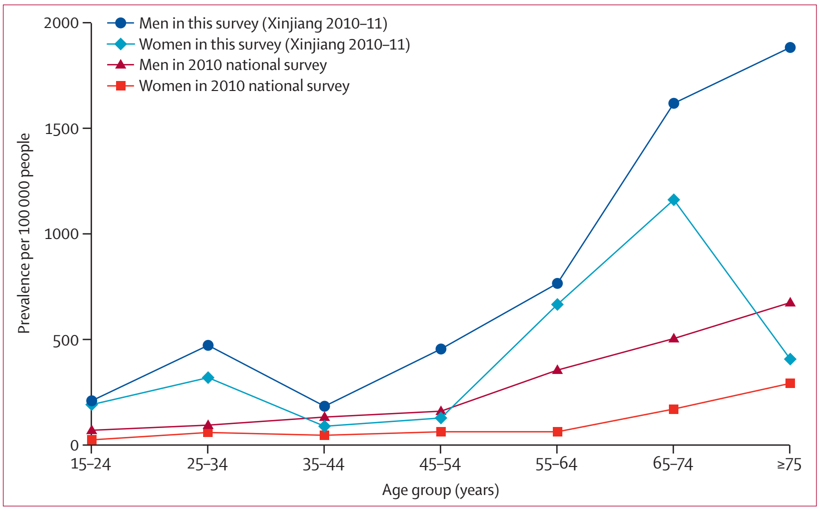

***Figure 5*: Age-specific prevalence of bacteriologically confirmed pulmonary tuberculosis stratified by sex in our Xinjiang survey and the 2010 national survey**
Prevalence in this survey age and sex standardised to the population of China in 2010.

on addressing the regional disparities, which exist both within and across the provinces, in the future.

With adjustment for survey strata, age, and ethnicity, men were still 1·31 times more likely to have bacteriologically confirmed pulmonary tuberculosis than were women in Xinjiang. Sex disparities in tuberculosis prevalence have been observed in many countries.[19] The effect of smoking, inequalities in socioeconomic status, differences in access to health care, and hormone-related differences in immunity between sexes have been reported in previous studies[20–22] as possible causes for the sex gap in tuberculosis prevalence. Additionally, we found that the PDR was substantially lower in men than in women, suggesting a low case detection rate or poor access to care among men compared with women.

Survey	Participation/ sample size	Clusters/ average size	Screening strategy		Screening positive	Smear positive	Bacterio-logically confirmed	MTB cultures recovered among smear positive	New or unknown smear positive	Prevalence of smear positive per 100 000 people (95% CI)	Prevalence of bacteriologically confirmed per 100 000 people (95% CI)	Overall PDR (95% CI)
			Symptom interview	Chest radiograph								
2000*	19 309/19 804 (97·5%)	19/1016	Cough or sputum production ≥3 weeks	Fluoroscopy, if abnormal, then radiography	631/19 309 (3·3%)	43/631 (6·8%)	67/618 (10·8%)	36/43 (83·7%)	25/631 (4·0%)	231 (148–314)	365 (237–493)	0·31 (0·21–0·47)
2011	29 835/31 081 (96·0%)	22/1356	Cough or sputum production ≥2 weeks or haemoptysis	Abnormal chest radiography	1607/29 835 (5·4%)	50/1589 (3·1%)	101/1589 (6·4%)	43/50 (86·0%)	37/1589 (2·3%)	170 (103–233)	430 (249–611)	0·34 (0·25–0·44)

Data are n/N (%) unless otherwise indicated. MTB=*Mycobacterium tuberculosis*. PDR=patient diagnosis rate. *Data from survey participants aged 15 years or older.

***Table 3*: Characteristics and results of 2000 and 2010–11 pulmonary tuberculosis surveys in Xinjiang, China**

	Notification rate for new smear-positive pulmonary tuberculosis (per 100 000 people)*	Prevalence of new smear-positive pulmonary tuberculosis (per 100 000 people)	PDR
Overall	42	124 (90–158)	0·34 (0·25–0·44)
Stratum			
Urban	17	23 (4–62)	0·74 (0·21–2·67)
Semi-urban	36	206 (134–278)	0·17 (0·12–0·25)
Rural	56	131 (73–189)	0·43 (0·28–0·67)
Sex			
Male	44	159 (121–196)	0·28 (0·22–0·35)
Female	39	91 (45–137)	0·43 (0·26–0·72)
Age group (years)			
15–24	35	81 (10–152)	0·43 (0·13–1·36)
25–34	34	185 (87–283)	0·18 (0·11–0·31)
35–44	21	70 (8–134)	0·30 (0·12–0·76)
45–54	33	114 (17–211)	0·29 (0·12–0·69)
55–64	84	191 (16–366)	0·44 (0·16–1·20)
65–74	112	116 (6–226)	0·97 (0·30–3·14)
≥75	111	229 (21–437)	0·48 (0·13–1·79)
Ethnic group			
Han	16	28 (1–55)	0·57 (0·21–1·47)
Uyghur	58	189 (132–246)	0·31 (0·23–0·42)
Others	63	145 (70–220)	0·43 (0·26–0·73)
Geographical location			
Eastern region	24	43 (3–83)	0·56 (0·20–1·66)
Northwestern region	39	97 (46–148)	0·40 (0·23–0·67)
Southern region	53	185 (121–249)	0·29 (0·26–0·31)

Data in parentheses are 95% CIs. PDR=patient diagnosis rate. *Data for notified new smear-positive pulmonary tuberculosis in 2011 was provided by Xinjiang CDC. Source of 2011 population size was Jianxin.[9]

***Table 4*: Estimated overall and specific PDRs in 2011**

Prevalence increased with age in both women and men. However, a particularly high prevalence of bacteriologically confirmed pulmonary tuberculosis was observed in the 25–34 years and 65–74 years age groups. This pattern is different from that seen in the 2010 national survey (figure 4, 5). A high prevalence in young adults might be due to a low case detection rate because the estimated PDR was lowest in those aged 25–34 years. HIV infection might be another potential cause of high pulmonary tuberculosis prevalence among young adults. HIV positivity was not tested in this survey; however, findings from a study in Xinjiang[23] revealed that HIV infection among 1501 patients with newly diagnosed tuberculosis was 14% and that most patients co-infected with HIV and tuberculosis were aged 25–34 years. Additionally, the HIV notification rate in Xinjiang in 2011 was substantially higher in this age group (appendix). These results suggest that HIV screening should be enhanced among patients with newly diagnosed tuberculosis, particularly in young adults. A high prevalence of pulmonary tuberculosis in elderly people might be due to age-related immune dysfunction[24] and other chronic comorbidities, such as diabetes.[25–27] However, some other biological and socio-economic factors might also explain the age variation. Additional qualitative studies are needed to understand the barriers to pulmonary tuberculosis screening and care in these high-risk populations.

We observed marked ethnic differences in prevalence in this survey. Prevalence among the Han ethnic group in Xinjiang was similar to that in the general population in the more developed eastern region of China.[3] However, individuals of the Uyghur ethnic group were 6·28 times more likely to have bacteriologically confirmed pulmonary tuberculosis than were the Han ethnic group, and other ethnic groups (including Kyrkiz, Kazakh, and Hui) were 4·34 times more likely. Ethnic disparities in prevalence have also been observed in other countries.[28,29] Low socioeconomic status, high HIV infection, poverty, and delayed diagnosis and treatment are potential reasons for the high prevalence among minority groups in Xinjiang.[30–32] However, we were unable to identify the underlying causes of ethnic disparity because relevant data were not collected. Study of the social, cultural, and biological determinants of tuberculosis infection in Xinjiang is an area for future research.

Although the PDR is not the same as the true case detection rate (as the true incidence of pulmonary tuberculosis is not known), a comparison of the PDR between populations or subpopulations can provide information about the relative completeness of case detection. The estimated overall PDR in Xinjiang was less than half of the national estimate in 2010 (0·34 *vs* 0·75)[33] and it increased only slightly since 2000, suggesting that a large number of tuberculosis cases remain undetected with the current DOTS-based passive case-finding strategy. Improved control strategies that enable early diagnosis and treatment, such as widening of the current screening criteria and use of new and rapid diagnostic tools, along with raised awareness of the magnitude and characteristics of tuberculosis cases in the community by health-care providers, are required. Young adults aged 25–34 years, men, and the Uyghur ethnic group should be prioritised for active case finding in future tuberculosis control programmes in Xinjiang.

After implementation of DOTS-based tuberculosis control programmes in the past 20 years, China achieved the 2015 Millennium Development Goal of a 50% reduction in tuberculosis prevalence.[34] However, regional disparities in tuberculosis burden in China should be addressed, particularly the high burden in poor western areas, to achieve the post-2015 global targets for tuberculosis control. Current financial and human resources in tuberculosis care in western China are inadequate. Sustained and adequate funding is needed to improve the availability, distribution, and motivation of competent tuberculosis health-care providers and strengthen the capacity of the laboratory network in the rural western region. Additional efforts are needed to identify and address the physical, social, and cultural barriers to early tuberculosis diagnosis and treatment in multiethnic western China. Considering the widespread poverty in western China, an urgent need exists for policies that reduce out-of-pocket payments from patients with tuberculosis directly or indirectly related to tuberculosis care that are not included in the so-called free tuberculosis care policy in current Chinese tuberculosis control programmes.

The findings in this survey are subject to several limitations. First, the eligible population did not include adults who were living in the survey cluster area for less than 6 months. Additionally, those registered residents in the survey cluster who moved out of the survey site more than 3 months before the survey were excluded. This mobile population, which tends to be young and predominantly male, might be expected to have a high risk of pulmonary tuberculosis on the basis of our findings. As such, our survey could underestimate pulmonary tuberculosis prevalence. Second, the symptom screening criteria that we used in this survey did not include other symptoms such as fever, night sweats, chest pain, and weight loss. Van't Hoog and colleagues[35] reported that use of any tuberculosis symptoms as the symptom screening criteria in a tuberculosis survey yielded higher sensitivity (90%) than that with use of cough for at least the past 2 weeks or haemoptysis (52%). Therefore, we might have missed some presumptive pulmonary tuberculosis cases and underestimated the prevalence in our survey. However, we used a screening strategy combining pulmonary tuberculosis symptoms and chest radiographs in our survey, which have a higher sensitivity than with symptom screening alone. This screening strategy was designed considering both the survey budget and workload of local laboratories and was used in the 2010 national survey and national tuberculosis control programmes of China.[36] Furthermore, the possibility of overdecontamination and degradation of sputum specimens during transportation might have caused an underestimation of the true number of culture-positive pulmonary tuberculosis cases.

Third, the estimate of smear-positive pulmonary tuberculosis prevalence was similar in the incomplete case analysis (method 1) and the individual analysis incorporating inverse probability weighting and multiple imputation of missing data (method 2). However, the difference in bacteriologically confirmed pulmonary tuberculosis prevalence between these two analyses was large, which could be due to a higher proportion of missing data for culture results than for smear results. Nonetheless, the analysis incorporating inverse probability weighting and multiple imputation might be the safest approach to correct the bias introduced by missing data and provides the best estimate of tuberculosis prevalence at the population level.[37,38] Finally, if people with tuberculosis cases had been tested for HIV, the role of HIV in the tuberculosis epidemic could have been better explained than was possible with this study. Further investigations are needed to guide public health strategies to reduce tuberculosis burden in this region.

We found a very high burden of pulmonary tuberculosis among adults in Xinjiang after implementation of the DOTS strategy for longer than 10 years. The very low PDR indicates a low case detection rate, limiting the effectiveness of the DOTS strategy. Large disparities exist between sex, age groups, geographical regions, and ethnic groups. Studies are urgently needed to understand the barriers to access to tuberculosis screening in this population to guide tuberculosis case-finding strategies targeting young men, the Uyghur ethnic group, and residents in semi-urban and rural areas. The tuberculosis epidemic in western China is a public health emergency that needs to be urgently addressed.

Contributors

LY, XF, and WG planned the research, developed the protocol, implemented the survey, and collected data. PM analysed data and wrote the first draft of the report. PJM, CM, and HU analysed and interpreted data and wrote the first draft of the report. LN and XF analysed and interpreted data. All authors critically reviewed the report and approved the final version.

Declaration of interests
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References
1 WHO. Global tuberculosis report 2015: 20th edition. Geneva: World Health Organization, 2015.

2 Hou WL, Song FJ, Zhang NX, et al. Implementation and community involvement in DOTS strategy: a systematic review of studies in China. *Int J Tuberc Lung Dis* 2012; **11:** 1433–40.

3 Wang L, Zhang H, Ruan Y, Chin DP, Xia Y, Cheng S. Tuberculosis prevalence in China, 1990–2010; a longitudinal analysis of national survey data. *Lancet* 2014; **383:** 2057–64.

4 Technical Guidance group of the Fifth National TB Epidemiological Survey; The office of the Fifth National TB Epidemiological Survey. The fifth national tuberculosis epidemiological survey in 2010. *Chin J Antituberculosis* 2012; **34:** 485–508 (in Chinese).

5 Jin X, Fan XC, Yan HK, et al. Report on the fourth epidemiological survey for tuberculosis in Xinjiang Uyghur Autonomous Region. *Chin J Antituberculosis* 2004; **26:** 264–67 (in Chinese).

6 Yang JM, Jieensi S, Yi XR, Li YH, Zhao Z. Analysis of tuberculosis epidemiological survey conducted in 2010–2011 in Xinjiang Uygur Autonomous Region. *Chin J Antituberculosis* 2013; **35:** 960–64 (in Chinese).

7 Hoa NB, Sy DN, Nhung NV, et al. National survey of tuberculosis prevalence in Viet Nam. *Bull World Health Organ* 2010; **88:** 273–80.

8 Borgdorff MW. New measurable indicator for tuberculosis case detection. *Emerg Infect Dis* 2004; **10:** 1523–28.

9 Jianxin J, ed. Xinjiang statistical yearbook. Beijing: China Statistics Press, 2011.

10 WHO. Tuberculosis prevalence surveys: a handbook. Geneva: World Health Organization, 2011.

11 Floyd S, Sismanidis C, Yamada N, et al. Analysis of tuberculosis prevalence surveys: new guidance on best-practice methods. *Emerg Themes Epidemiol* 2013; **10:** 10.

12 White IR, Royston P, Wood AM. Multiple imputation using chained equations: issues and guidance for practice. *Stat Med* 2011; **30:** 377–99.

13 Thompson ML, Myers JE, Kriebel D. Prevalence odds ratio or prevalence ratio in the analysis of cross sectional data: what is to be done? *Occup Environ Med* 1998; **4:** 272–77.

14 China Tuberculosis Control Collaboration. The effect of tuberculosis control in China. *Lancet* 2004; **364:** 417–22.

15 Xia YY, Du X, Cheng W, et al. Pulmonary tuberculosis prevalence among different regions in China in 2010. *Chin J Antituberculosis* 2012; **34:** 803–07 (in Chinese).

16 Jia Z, Cheng S, Wang L. Tuberculosis control in China: striving for sustainability. *Lancet* 2012; **9832:** 2149.

17 Du J, Pang Y, Liu Y, Mi F, Xu S, Li L. Survey of tuberculosis hospitals in China: current status and challenges. *PLoS One* 2014; **9:** e111945.

18 Jackson S, Sleigh AC, Wang GJ, Liu XL. Poverty and the economic effects of TB in rural China. *Int J Tuberc Lung Dis* 2006; **10:** 1104–10.

19 Rhines AS. The role of sex differences in the prevalence and transmission of tuberculosis. *Tuberculosis (Edinb)* 2013; **1:** 104–07.

20 Yamasaki-Nakagawa M, Ozasa K, Yamada N, et al. Gender difference in delays to diagnosis and health care seeking behaviour in a rural area of Nepal. *Int J Tuberc Lung Dis* 2001; **5:** 24–31.

21 Neyrolles O, Quintana-Murci L. Sexual inequality in tuberculosis. *PLoS Med* 2009; **6:** e1000199.

22 Nhamoyebonde S, Leslie A. Biological differences between the sexes and susceptibility to tuberculosis. *J Infect Dis* 2014; **209** (suppl 3)**:** S100–06.

23 Chen YG, Lu J, Ma Li, Liu H, Zhang WS. Survey on the tuberculosis (TB)/HIV co-infection situation in Urumqi. *J Modern Prev Med* 2012; **39:** 5410–12.

24 Castle SC. Clinical relevance of age-related immune dysfunction. *Clin Infect Dis* 2000; **31:** 578–85.

25 Restrepo BI, Schlesinger LS. Impact of diabetes on the natural history of tuberculosis. *Diabetes Res Clin Pract* 2014; **106:** 191–99.

26 Wang HT, Zhang J, Ji LC, et al. Frequency of tuberculosis among diabetic patients in the People's Republic of China. *Ther Clin Risk Manag* 2014; **10:** 45–49.

27 Yang YN, Xie X, Ma YT, et al. Type 2 diabetes in Xinjiang Uygur Autonomous Region, China. *PLoS One* 2012; **7:** e35270.

28 Centers for Disease Control and Prevention (CDC). Racial disparities in tuberculosis—selected southeastern states, 1991–2002. *MMWR Morb Mortal Wkly Rep* 2004; **53:** 556–59.

29 Raj P, Prakash R, Mishra G, et al. Prevalence of smear-positive pulmonary tuberculosis in different ethnic groups in India: evaluation of public health. *Public Health* 2012; **126:** 295–99.

30 Qi YC, Ma MJ, Li DJ, et al. Multidrug-resistant and extensively drug-resistant tuberculosis in multi-ethnic region, Xinjiang Uygur Autonomous Region, China. *PLoS One* 2012; **7:** e32103.

31 Liu FM, Gu XM, Yang JM, et al. Analysis on impacting factors on the failures in referring suspected TB patients reported and referred in Kashi Prefecture of Xinjiang Uygur Autonomous Region. *Chin J Antituberculosis* 2013; **35:** 54–59 (in Chinese).

32 Liu EY, Zhou L, Wang HF, Du X, Cheng SM. Characteristics of registered pulmonary tuberculosis patients in ethnic minority population in 2009. *Chin J Antituberculosis* 2011; **33:** 323–27 (in Chinese).

33 Xia YY, Cheng J, Zhang H, et al. Ratio of new smear positive tuberculosis notification and prevalence rate in different population and regions of China in 2010. *Chin J Antituberculosis* 2014; **36:** 498–502 (in Chinese).

34 Huynh GH, Klein DJ, Chin DP, et al. Tuberculosis control strategies to reach the 2035 global targets in China: the role of changing demographics and reactivation disease. *BMC Med* 2015; **13:** 88.

35 van't Hoog AH, Meme HK, Laserson KF, et al. Screening strategies for tuberculosis prevalence surveys: the value of chest radiography and symptoms. *PLoS One* 2012; **7:** e38691.

36 Cheng J, Wang L, Zhang H, Xia Y. Diagnostic value of symptom screening for pulmonary tuberculosis in China. *PLoS One* 2015; **5:** e0127725.

37 Sterne JA, White IR, Carlin JB, et al. Multiple imputation for missing data in epidemiological and clinical research: potential and pitfalls. *BMJ* 2009; **338:** b2393.

38 Seaman SR, White IR, Copas AJ, Li L. Combining multiple imputation and inverse-probability weighting. *Biometrics* 2012; **68:** 129–37.